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1. (Amended) A method of detecting a disease or a disease susceptibility trait in an organism, wherein said disease or said disease susceptibility trait is associated with a germline mutation in a subject gene, comprising:

- (a) isolating a normal biological sample from said organism;
- (b) immunologically quantitating the amount of wild-type protein expressed by said subject gene in said sample, and the amount of a reference protein expressed by a second gene in said sample;
- (c) calculating the ratio of the amount of the wild-type protein expressed by said subject gene in said sample to the amount of the reference protein expressed by said second gene in said sample;
- (d) determining whether or not said calculated ratio reflects an abnormally low level of said wild-type protein expressed by said subject gene in said sample; and
- (e) concluding, that if the ratio calculated in step (c) indicates that there is an abnormally low level of wild-type protein in said sample, that said subject gene contains a germline mutation in one of its alleles, and that the subject organism is affected by the disease or the disease susceptibility trait associated with said germline mutation.

**Please replace Claim 9 on page 61, lines 12-15 with the following new Claim 9**

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9. (Amended) The method according to Claim 1 wherein said biological sample is selected from the group consisting of body fluids, tissue specimens, tissue extracts, normal cells, lysates of normal cells, normal cell extracts, and supernatants from lysates of normal cells.

**Please replace Claims 11 and 12 on page 61, lines 23-30 with the following new Claims 11 and 12**

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11. (Amended) The method according to Claim 9 wherein the cells are peripheral blood lymphocytes; the cell lysates are lysates of peripheral blood lymphocytes; the cell extracts are from peripheral blood lymphocytes; and the supernatants are from lysates of peripheral blood lymphocytes.

12. (Amended) The method of Claim 1 wherein said biological sample is selected from the group consisting of normal cells, lysates of normal cells, and supernatants from lysates of normal cells.

**Please replace Claims 14 and 15 on page 62, lines 4-11 with the following new Claims 14 and 15**

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14. (Amended) The method of Claim 1 wherein said germline mutation is selected from the group consisting of truncating-causing mutations and mutations that cause allelic loss.

15. (Amended) The method of Claim 14 wherein said mutation is selected from the group consisting of nonsense mutations, frameshift mutations, promoter mutations, enhancer mutations, splice site mutations, null mutations, and poly-A tail mutations.

Please replace Claim 24, page 63, line 21 to page 64, line 11 with the following new Claim 24

24. (Amended) A method of detecting a disease or a disease susceptibility trait in an organism, wherein said disease or said disease susceptibility trait is associated with a germline mutation in one of two or more subject genes, comprising:

(a) isolating a normal biological sample from said organism;

(b) immunologically quantitating the amount of wild-type protein in said sample, that is expressed by each of the subject genes;

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(c) calculating the ratio of the amount of the wild-type protein expressed by one of said subject genes in said sample, to the amount of wild-type protein expressed by the other subject gene in said sample, or to each of the amounts of wild-type protein expressed by each of the other subject genes in said sample;

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(d) determining whether the ratio or ratios calculated in step (c) reflects or reflect an abnormally low level of a wild-type protein expressed by either of the subject genes, or by any of the subject genes in said sample; and

(e) concluding that if the ratio or ratios calculated in step (c) indicates or indicate that there is an abnormally low level of a wild-type protein expressed by one of the subject genes in said sample, that that subject gene contains a germline mutation in one of its alleles, and that the subject organism is affected by the disease or the disease susceptibility trait associated with said germline mutation.

**Please replace Claims 31-33, page 65, lines 1-13 with the following new Claims 31-33**

31. (Amended) The method of Claim 24 wherein said mutation is selected from the group consisting of truncating-causing mutations and mutations that cause allelic loss.

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32. (Amended) The method of Claim 31 wherein said mutation is selected from the group consisting of nonsense mutations, frameshift mutations, promoter mutations, enhancer mutations, splice site mutations, null mutations, and poly-A tail mutations.

33. (Amended) The method of Claim 24 wherein said biological sample is selected from the group consisting of body fluids, tissue specimens, tissue extracts, normal cells, lysates of normal cells, normal cell extracts, and supernatants from lysates of normal cells.

**Please replace Claims 35 and 36, page 65, lines 21-28 with the following new Claims 35 and 36**

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35. (Amended) The method of Claim 33 wherein the cells are peripheral blood lymphocytes; the cell lysates are lysates of peripheral blood lymphocytes; the cell extracts are from peripheral blood lymphocytes; and the supernatants are from lysates of peripheral blood lymphocytes.

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36. (Amended) The method of Claim 24 wherein said biological sample is selected from the group consisting of normal cells, lysates of normal cells, and supernatants from lysates of normal cells.

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**Please replace Claim 45, page 67, lines 6-22 with the following new Claim 45**

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45. (Amended) A method of detecting a disease or a disease susceptibility trait in an organism, wherein said disease or said disease susceptibility trait is associated with a germline mutation in a subject gene, comprising:

(a) isolating a sample of normal cells from said organism;  
(b) immunologically quantitating the amount of wild-type protein expressed by the subject gene in said sample;

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(c) determining whether the amount of wild-type protein present in said sample is abnormally low in comparison to the amount of wild-type protein expressed by the subject gene in a control sample; and

(d) if the amount of said wild-type protein in said sample is determined to be abnormally low in comparison to the amount of wild-type protein in the control sample, concluding that the subject gene has a mutation in one allele, and correlating the conclusion with the subject organism having the disease or the disease susceptibility trait associated with said germline mutation.

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**Please insert new Claims 49-54**

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49. A method according to Claim 1 wherein the abnormally low level of the wild-type protein is 50%  $\pm$  20% of the level of said protein in comparable samples from

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organisms unaffected by said disease or said disease susceptibility trait associated with said germline mutation, wherein said unaffected organisms are of the same taxonomic classification as the subject organism.

50. A method according to Claim 49 wherein the abnormally low level of said wild-type protein is  $50\% \pm 15\%$  of the level of said protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.

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51. A method according to Claim 49 wherein the abnormally low level of said wild-type protein is  $50\% \pm 10\%$  of the level of said protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.

52. A method according to Claim 49 wherein the abnormally low level of said wild-type protein is about 50% of the level of said wild-type protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.

53. A method according to Claim 2 wherein the ratio calculated in step (c) when compared to said mean of ratios indicates that said abnormally low level of said wild-type protein expressed by said subject gene is about 50% of the level of said wild-type protein in comparable samples from organisms unaffected by said disease or said disease susceptibility trait.